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GREEN FACTOR

Cell-Free Biomanufacturing



SUMMARY

Los Alamos is designing a screening platform coupled to our biosensor to customize production processes in cell-free environments that offer biomanufacturers higher titers and yields, better resource utilization and cost-effective bioprocess. Our technology aims at enabling cell-free biosynthetic systems by providing enzyme variants generated by coupling with our biosensor technology, that can utilize cheap raw material cofactor analogues. This will enable bioprocesses based on cell free synthetic biology for a sustainable bioeconomy.



MARKET

The synthetic biology market is growing rapidly representing several markets, including biofuels, biopolymers & bioplastics, commodity chemicals, food and nutrition, pharma and healthcare, cosmetics, genomics and DNA synthesis. The \$13.3B market is increasing with a CAGR of greater than 25% globally as new bioprocesses are becoming increasingly competitive with oil-based manufacturing processes. Our technology is a building block platform that targets and replaces expensive raw materials in the manufacturing process. New, affordable raw material cofactor analogues can be utilized by manufacturers in every synthetic biology manufacturing process, impacting products like bio-nylon, bio-PET, vanilla, and many more.

BENEFITS

Cell-free systems have emerged as the viable method to produce bio-based products for a sustainable future to meet the needs of the expanding human population. Our technology offers many advantages over oil-based manufacturing as well as cell-based processes in synthetic biology, including:

- Cost effective process with cheaper cofactor analogues
- Faster prototyping, scalability and purity due to elimination of side reactions
- Ability to adapt to a variety of metabolic pathways, alternate feedstocks and products even those that are toxic and give solvent intolerance.
- Higher carbon conversion efficiency, yields and titers.
- Better control of reactions and enable enzyme reactions consortia to functionalize novel biosynthetic pathways.

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WHY WE ARE BUILDING GREEN FACTOR

Synthetic biology has made it possible to make virtually any molecule by assembling DNA parts. However, when living cells are used in the bioprocess, the requirements of their growth and maintenance often conflict with the production of the end-product target molecule, such as bio-nylon. As a result, the cells go through poor physiology and low product titers. Synthetic biology in cell-free systems have evolved as a key potential platform to decouple cell growth from biocatalyst synthesis. Certain raw materials requirements in a biosynthetic pathway such as cofactors, add high costs to the bioprocess. Cofactor supply, regeneration and instability remains a significant challenge in cell-free metabolic engineering. Our technology aims at better utilizing inexpensive cofactor analogues by enabling enzyme modifications to ensure that the bioprocesses are cost effective and economically viable. Cell-free systems can take advantage of many renewable feedstocks like the abundant agricultural residues and environmental pollutants.



WHAT'S BEHIND OUR TECHNOLOGY

Los Alamos has proven significant yield improvements in cell-based solutions to improve the manufacturing economics in bio-nylon. We are now applying enzyme modifications by generating libraries and coupling them to our small molecule biosensor technology to screen for the best enzyme variants that can utilize cheap cofactors using a cell-free system. We are aiming for as much as 90% yield improvements in bio-nylon production. This specific cofactor analogue can be applied to many other product manufacturing processes.



OUR COMPETITIVE ADVANTAGES

Our technology offers significant cost reductions in biomanufacturing by replacing expensive cofactors. Because we decouple the growth from the biocatalysis this significantly increases the yields and efficiencies of the bioprocess. Leveraging this technology in a cell-free system allows for scalability and purity.



OUR TECHNOLOGY STATUS

Our group has developed in-vivo biosensors called 'Smart microbial cell technology' for small molecules. This technology has an improved version of an enzyme in an important biosynthetic pathway used for bioplastics manufacturing (Jha et al., 2019). This technology is also being used to improve the microbial strain used for biomanufacturing and identify non-intuitive mutations (Bentley et al., 2020). We are currently coupling these genetic biosensors in a cell-free system to identify alternate raw material analogues, their utilization by enzymes, and variations needed to accomplish this and enable cost viable cell free bioprocess.



PUBLICATIONS AND IP

1. Smart Microbial Cell Technology. 2020
2. Bentley et al. Metabolic Engineering. 2020
3. Jha et al. ACS Synthetic Biology. 2019